Alcon
RESEARCH, LTD.

6201 SOUTH FREEWAY
FORT WORTH, TEXAS 76134-2099
(817) 293-0450

May 8, 2000

Dockets Management Branch
(HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: Docket No. 93D-0139

To Whom It May Concern:

Alcon Research, Ltd. is providing the attached comments on the draft revised guidance entitled "Q1A(R) Stability Testing of New Drug Substances and Products" which was published in the April 21, 2000 Federal Register. This submission is provided in duplicate.

Sincerely,

Rebecca G. Walker
Senior Director, Regulatory Compliance

RGW:ss

Attachment

cc: Brian Matthews
Richard Johnson

93D-0139

C 48

Docket No. 93D-0139
Draft Revised Guidance:
"Q1A Stability Testing of New Drug Substances and Products"

The modifications to the original guidance (published in the **Federal Register** of September 22, 1994) are to a large extent welcomed; in particular, the additional clarity of the testing requirements for products in semi-permeable containers is welcomed. The option to use alternative storage conditions for products in semi-permeable containers and the use of 'ratios' is applauded. Furthermore, the clarification that products in impermeable containers can be stored under any humidity conditions is considered to be reasonable.

However, it is noted that there is disparity between this guidance and the draft guidance published in the **Federal Register** of June 8, 1998, "Stability Testing of Drug Substances and Drug Products." It is hoped that clarity will be provided by the Agency on which set of information industry will be able to rely as guidance.

SPECIFIC COMMENTS

Products packaged in semi-permeable containers (Page 21451)

Storage conditions

There is disparity between this guidance and the draft guidance, "Stability Testing of Drug Substances and Drug Products" published in the **Federal Register** June 8, 1998. Clarification of which set of information the agency is advocating is needed:

This draft guidance:
Long-term: 25° C +/- 2°C / 40% RH +/- 5%
Intermediate: 30°C +/- 2°C / 60% RH +/- 5%
Accelerated: 40°C +/- 2°C / NMT 25%

FDA draft guidance published June 8, 1998:
Long-term: 25°C +/- 2°C / 40% RH +/- 5%
Intermediate: 30°C +/- 2°C / 40% RH +/- 5%
Accelerated: 40°C +/- 2°C / 15% RH +/-5%

Water loss determination period

In practice, the data collected over a three month period frequently show greater variability than data collected over a period of six months. It is proposed that the water vapor loss data should be collected over a six-month period, and that the limit be suitably amended.

'Small single dose products'

The clear exemption to the need to undertake testing under intermediate conditions solely on the basis of moisture loss rate with small volume containers is noted and welcomed. However, the following points are made:

1. 'Small' is not defined: This omission is likely to result in different interpretations by different entities and therefore it is proposed that 'small' be defined (e.g., '1 mL or less').

2. The limitation of this relaxation to product used to deliver a single dose is unnecessarily restrictive. Small volume containers can be used to deliver more than one dose, (e.g., one dose to each eye on one occasion, or even more than one dose to one eye provided that appropriate data

are provided to justify such usage.) It is therefore proposed that the term used in the guidance be 'small volume containers (*x* mL or less)'.

Testing: Labeled or unlabeled product; and overwrapped or unwrapped product

For small volume product in semi-permeable containers (such as eye drops) the data for water vapor loss rate obtained with labeled containers and with unlabeled containers can differ significantly. It would be helpful if it could be indicated whether product should be tested in the labeled or unlabeled state.

For very small volume products it is not unusual to test the product with an overwrap in place. It is assumed that this is appropriate for long-term testing (because the overwrapped product is what is placed on the market). The performance of the individual units once removed from the overwrap is more appropriate to in-use stability testing protocols. It would be helpful if this could be confirmed in the guidance.

The need for product-specific studies for moisture vapor loss

The water vapor permeability for a given container system (design and materials of construction) are independent of the product provided that the physical characteristics of the product which affect vapor pressure are similar. This, for example, is the case for the majority of ophthalmic products. Therefore, where the same container system is used and the products have comparable characteristics it would appear to be reasonable to accept weight loss data on related products rather than to require specific studies on each product (which simply duplicates effort).

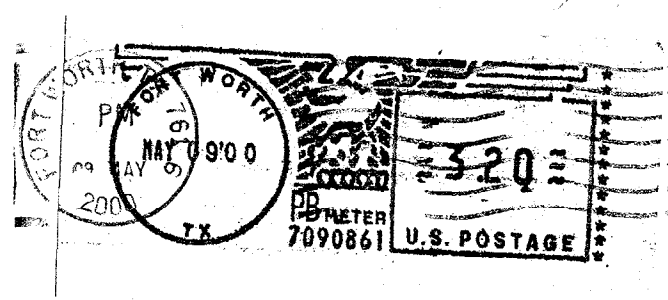
Alcon

ALCON RESEARCH, LTD.
6201 SOUTH FWY
FORT WORTH TX 76134-2099

CERTIFIED

Z 434 352 166

MAIL



Dockets Management Branch
(HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

20857-0001